

Application Ser. No.: 10/635,048
Title: GLYCINE BETAINES AND ITS USE
Response to Office Action dated: December 6, 2005

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Amended claims without prejudice

1. (Withdrawn) A pharmaceutical antithrombotic combination comprising:
 - (a) a therapeutically effective amount of a therapeutically antithrombotic active agent causing at least one haemorrhagic side effect, said active agent being selected from the group consisting of anti aggregants selected from the group consisting of abciximab, acetylsalicylate basic aluminium, acetylsalicylate carbonate sodium, acetylsalicylate lysine, acetylsalicylic acid, aloxiprine, anagrelide hydrochloride, bencyclane furamate, carbasalate calcium, clopidogrel sulfate, epoprostenol sodium, epifibatide, hydroxychloroquine sulfate, iloprost, nicergoline, nifedipine, pyricarbate, sulfinpyrazone, ticlopidine hydrochloride, tirofiban hydrochloride, verapamil hydrochloride, compounds structurally similar to one of said preceding anti aggregant compounds, and mixtures thereof, anticoagulants selected from the group consisting of acenocoumarol, anisindione, biscoumacetate ethyl, bromindione, coumatetralol, sirudine, oxazindione, phenindione, phenprocoumon, ticlopidine, warfarine sodium, compounds structurally similar to one of the preceding anti coagulant compounds, and mixtures thereof, fibrinolytics selected from the group consisting of alteplase, anistreplase, atorvastatin calcium, bromelaines, ciprofibrate, defibrotide, fluvastatin sodium, glicazide, lovastatin, lys-plasminogen, phenformin, pravastatin sodium, reteplase, simvastatin, streptokinase, urokinase, compounds structurally similar to one of the preceding fibrinolytic compounds, and mixtures thereof, thrombin inhibitors, anti vitamin K, and mixtures thereof; and
 - (b) a therapeutically effective amount of a compound selected from the group consisting of compounds of the formula $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$ with n an integer from 1 to 5, pharmaceutically acceptable salts thereof, esters thereof, precursors thereof, and mixtures thereof,said combination operable for preventing or reducing the incidence or severity of said haemorrhagic side effect or for potentialising the therapeutic antithrombotic effect of said antithrombotic active agent.
2. (Withdrawn) The pharmaceutical combination of claim 1, said compound being selected from the group consisting of glycine betaine, pharmaceutically acceptable salts thereof, esters thereof, precursors thereof, and mixtures thereof.

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3. (Withdrawn) The pharmaceutical combination of claim 1, in which the therapeutic antithrombotic active agent has at least possible haemorrhagic side effects, and in which the combination comprises a therapeutically effective amount of glycine betaine for preventing or reducing the incidence or severity of said haemorrhagic side effect.

4. (Withdrawn) The pharmaceutical combination of claim 3, in which said glycine betaine is in a form selected from the group consisting of forms suitable for subcutaneous injection and forms suitable for the preparation of a form for subcutaneous injection.

5. (Withdrawn) The pharmaceutical combination of claim 1, in which the therapeutic antithrombotic agent with at least possible side effect is selected from the group consisting of anti vitamin K, antiaggregants, anticoagulants, anti thrombin, fibrinolytics and mixtures thereof.

6. (Withdrawn) The pharmaceutical combination of claim 1, in which the therapeutic antithrombotic active agent with possible side effect and glycine betaine are in a form selected from the group consisting of a form suitable for simultaneous administration, a form suitable for successive administration, and a form suitable for administration according to different administration paths.

7. (Withdrawn) The pharmaceutical combination of claim 1, in which the therapeutic antithrombotic active agent has at least one possible haemorrhagic side effect, and in which the combination comprises a therapeutically effective amount of glycine betaine for completely preventing said haemorrhagic side effect.

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8. (Withdrawn) A method of preventing side effects associated with an active agent selected from the group consisting of anti aggregants selected from the group consisting of abciximab, acetylsalicylate basic aluminium, acetylsalicylate carbonate sodium, acetylsalicylate lysine, acetylsalicylic acid, aloxiprine, anagrelide hydrochloride, benzocyclane furanate, carbasalate calcium, clopidogrel sulfate, epoprostenol sodium, epifibatide, hydroxychloroquine sulfate, iloprost, nicergoline, nifedipine, pyricarbate, sulfinpyrazone, ticlopidine hydrochloride, tirofiban hydrochloride, verapamil hydrochloride, compounds structurally similar to one of the preceding anti aggregant compounds, and mixtures thereof, anticoagulants selected from the group consisting of acenocoumarol, anisindione, bismacacetate ethyl, bromindione, coumatetral, dalteparin sodium, hirudin, xiran sulfate, enoxaparin sodium, fluindione, heparinate magnesium, heparin calcium, heparin sodium, lepirudin nadroparin calcium, oxazindione, pentosan polysulfate, phenindione, phenprocoumon, reviparin sodium, tinzaparin sodium, ticlofenac, warfarin sodium, glycoaminoglycans, heparins, unfractionated heparin, standard heparin, low molecular heparins, heparinoids, heparin-like molecules, compounds structurally similar to one of the preceding anti coagulant compounds, and mixtures thereof, fibrinolytics selected from the group consisting of alteplase, anistreplase, atorvastatin calcium, bromelains, ciprofibrate, defibrotide, fluvastatin sodium, glicazide, lovastatin, lys-plasminogen, phenformin, pravastatin sodium, reteplase, simvastatin, streptokinase, urokinase, compounds structurally similar to one of the preceding fibrinolytic compounds, and mixtures thereof, thrombin inhibitors such as argatroban, novastan, and mixtures thereof, anti vitamin K, and mixtures thereof, said method comprising the step of:

administering an antidote composition comprising an active antidote agent compound selected from the group consisting of glycine betaine, compounds of the formula $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$ with n being an integer from 1 to 5, pharmaceutically acceptable salts of said compound, esters of said compound, precursors of said compound, and mixtures thereof.

9. (Withdrawn) A method of preventing or reducing the incidence or severity of a side effect of a therapeutically active agent having at least one possible haemorrhagic side effect in a patient comprising the step of:

administering to said patient an effective amount of a compound selected from the group consisting of compounds having the formula $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$ with n being an integer from 1 to 5, pharmaceutically acceptable salts of said compound, esters of said compound, precursors of said compound, and mixtures thereof, said administration preventing or reducing the incidence or severity of said side effect or potentialising the therapeutic effect of said therapeutically active agent.

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10. (Withdrawn) The method of claim 9, said compound comprising glycine betaine, and said administration of said compound preventing or reducing the incidence or severity of said side effect and potentializing the therapeutic effect of said therapeutically active agent.

11. (Withdrawn) A method of potentializing the therapeutic effect of a therapeutically active agent having at least one possible haemorrhagic side effect in a patient comprising the step of:

administering to said patient an effective amount of a compound selected from the group consisting of glycine betaine, compounds having the formula $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$ with n being an integer from 1 to 5, pharmaceutically acceptable salts of said compound, esters of said compound, precursors of said compound, and mixtures thereof.

12. (Withdrawn) A method of treating or preventing thrombosis troubles for a patient and preventing or reducing a haemorrhagic side effect comprising the steps of:

administering to said patient a therapeutically effective amount of an anti thrombotic active agent with at least one possible haemorrhagic side effect; and
administering a therapeutic effective amount of glycine betaine to said patient and thereby preventing or reducing said haemorrhagic side effect.

13. (Withdrawn) The method of claim 12 said glycine betaine being subcutaneously injected.

14. (Currently amended) A controlled release pharmaceutical system suitable for delivering after administration in a time-controlled manner to the bloodstream of a mammal a ~~compound selected from the group consisting of glycine betaine, or comprising~~ an effective amount of [[a]] an active compound selected from the group consisting of a compound of formula $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$ with n equal to 1, glycine betaine, [[or a]] pharmaceutically acceptable salts thereof, ~~esters thereof~~, precursors thereof, and mixtures thereof.

15. (Original) The system of claim 14, said system being selected from the group consisting of oral controlled release preparations, oral controlled release devices, transdermal controlled release preparations, transdermal controlled release devices, and combinations thereof.

16. (Original) The system of claim 14, said system operable for releasing glycine betaine as an active ingredient.

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17. (Currently amended) The system of claim 14 wherein said system comprises at least one electronic element selected from the group consisting of an electronic device ~~[[or]] and~~ chip, said at least one element ~~electronic device or chip~~ operable for controlling at least ~~[[one]]~~ the releasing system or device of the active compound.

18. (Original) The system of claim 14, said system controlling delivery of said compound for at least about 120 minutes.

19. (Currently amended) A controlled release pharmaceutical system for achieving a goal selected from the group consisting of treating a condition, reducing the incidence of a condition, ~~[[or]]~~ reducing the severity of a condition, ~~[[or]]~~ and preventing a condition, whereby said condition is selected from the group consisting of blood flow disturbances, thrombosis, thromboembolic disorders, and combinations thereof, said system being adapted for releasing in a time controlled manner for at least 120 minutes, after administration, a therapeutically effective amount of an active compound selected from the group consisting of glycine betaine, a compound of formula $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$ with n equal to 1, pharmaceutically acceptable salts of said compound, ~~esters of said compound~~, precursors of said compounds, and mixtures thereof.

20. (Currently amended) The system of claim 19 wherein said system comprises at least one electronic device or chip, said at least one electronic element selected from the group consisting of an electronic device ~~[[or]] and~~ chip, said at least one electronic element being operable for controlling at least ~~[[one]]~~ the releasing system or device release of the active compound.

21. (Original) The system of claim 19, said system being an oral controlled release pharmaceutical system.

22. (Currently amended) The system of claim 19 wherein said system comprises at least one electronic element selected from the group consisting of an electronic device ~~[[or]] and~~ chip, said element being operable for controlling ~~at least one releasing system or device~~ the release of the active compound.

23. (Currently amended) The system of claim 19, wherein the system is adapted for controlling the release of said active compound ~~is controlled~~ for at least for 180 minutes.

24. (Currently amended) The system of claim 19, wherein the system is adapted for controlling the release of said active compound ~~[[is controlled]]~~ for at least for 240 minutes.

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25. (Currently amended) The system of claim 19, wherein the system is adapted for controlling the release of said active compound ~~[[is controlled]]~~ for at least for 360 minutes.

26. (Currently amended) The system of claim 19, wherein the system is adapted for controlling the release of said active compound ~~[[is controlled]]~~ for at least for 2160 minutes.

27. (Currently amended) A controlled release pharmaceutical system for releasing an effective therapeutic amount of a compound selected from the group consisting of betaines, pharmaceutically acceptable salts thereof, ~~[[esters thereof,]]~~ precursors thereof, and mixtures thereof, wherein said system is adapted for controlling ~~[[controls]]~~ for at least 120 minutes the release of ~~a glycine betaine or~~ an effective amount of a compound of formula $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$ with n equal to 1, glycine betaine, pharmaceutically acceptable salts thereof, ~~[[esters thereof,]]~~ precursors thereof, and mixtures thereof.

28. (Currently amended) The system of claim 27, in which the system is adapted for controlling ~~[[controls]]~~ at least for 180 minutes the release of ~~at least a glycine betaine or~~ an effective amount of a compound selected from the group consisting of a compound of formula $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$ with n equal to 1, pharmaceutically acceptable salts thereof, ~~[[esters thereof,]]~~ precursors thereof, and mixtures thereof.

29. (Currently amended) The system of claim 27, in which the system is adapted for controlling ~~[[controls]]~~ the release of ~~at least a glycine betaine or~~ an effective amount of a compound selected from the group consisting of a compound of formula $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$ with n equal to 1, glycine betaine, pharmaceutically acceptable salts thereof, ~~[[esters thereof,]]~~ precursors thereof, ~~precursors thereof, precursors thereof,~~ and mixtures thereof for between about 240 minutes and 2160 minutes.

30. (Currently amended) The system of claim 27 wherein said system comprises at least one electronic element selected from the group consisting of an electronic device ~~[[or]]~~ and chip, said element being operable for controlling at least one releasing system or device the release of the active compound.

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31. (Withdrawn) A method for treating, reducing the incidence or severity of, or preventing a condition selected from the group consisting of blood flow disturbances, thrombosis, thromboembolic disorders, and combinations thereof, said method comprising the step of administering in a time controlled manner to the bloodstream of a mammal, a therapeutically effective amount of an active selected from the group consisting of glycine betaine, a compound of the formula $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$ with n equal to 1, pharmaceutically acceptable salts of said compound, esters of said compound, precursors of said compound, and mixtures thereof.

32. (Withdrawn) The method of claim 31, said administration being transdermal.

33. (Withdrawn) A pharmaceutical combination for oral, parenteral or rectal administration comprising:

a therapeutically effective amount of a therapeutically active agent causing at least one haemorrhagic side effect, said active agent being selected from the group consisting of dalteparine sodium, sirudine, xtran sulfate, enoxaparine sodium, fluindione, heparinate magnesium, heparin calcium, heparine sodium, lepirudine nadroparine calcium, pentosane polyester sulfuric, reviparine sodium, tinzaparine sodium, glycoaminoglycans, heparins, unfractionated heparin, standard heparin, low molecular heparins, heparinoids, heparin-like molecules, compounds structurally similar to one of the preceding anti coagulant compounds, and mixtures thereof; and

a therapeutically effective amount of a compound selected from the group consisting of glycine betaine, $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$ with n being an integer from 1 to 5, pharmaceutically acceptable salts thereof, esters thereof, precursors thereof, and mixtures thereof,

said combination preventing or reducing the incidence or severity of said haemorrhagic side effect or potentialising the therapeutic effect of said active agent.

34. (Withdrawn) The pharmaceutical combination of claim 33, wherein said therapeutically active agent has at least possible haemorrhagic side effects, and in which said combination comprises a therapeutically effective amount of glycine betaine for preventing or reducing the incidence or severity of said haemorrhagic side effect.

35. (Withdrawn) The pharmaceutical combination of claim 33, said glycine betaine being in a form suitable for subcutaneous injection or in a form suitable for the preparation of a form for subcutaneous injection.

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36. (Withdrawn) The pharmaceutical combination of claim 33, said combination preventing or reducing the incidence or severity of said haemorrhagic side effect and potentialising the therapeutic effect of said active agent.

37. (Withdrawn) The pharmaceutical combination of claim 33, said therapeutically active agent being an antithrombotic agent with possible side effects, and said glycine betaine and said therapeutically active agent each being in a form suitable for simultaneous administration or successive administration or for administration according to different paths.

38. (Withdrawn) A method of treating a patient comprising the steps of:
administering to said patient an effective amount of a therapeutic active agent with at least one possible haemorrhagic side effect, and
administering to said patient an effective amount of a compound selected from the group consisting of compounds of the formula $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$ with n being an integer from 1 to 5, pharmaceutically acceptable salts thereof, esters thereof, precursors thereof, and mixtures thereof, wherein administration of said compound prevents or reduces the incidence or severity of said at least one side effect of said therapeutically active agent or potentializes the therapeutic effect of said therapeutically active agent.

39. (Withdrawn) The method of claim 38, said compound comprising an effective amount of glycine betaine.

40. (Withdrawn) A method for treating or preventing at least one trouble selected from the group consisting of blood flow disturbance, thrombosis, thromboembolic disorders and combinations thereof comprising the step of administering to the bloodstream of a mammal in a controlled manner a therapeutically effective amount of a compound selected from the group consisting of glycine betaine, compounds of the formula $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_n\text{COO}^-$ with n being an integer from 1 to 5, pharmaceutically acceptable salts thereof, esters thereof, precursors thereof, and mixtures thereof.

41. (Withdrawn) The method of claim 40, said administration being transdermal.